

D-2929 CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application of:)
Roger Aoki et al.)
Serial No. Pending) Examiner: N/A
Filed: Herewith) Art Unit: N/A
For: MULTIPLE BOTULINUM TOXINS)
FOR TREATING NEUROMUSCULAR)
DISORDERS AND CONDITIONS)

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on April 30, 2001.

Signed:

Jean F. Heuler

Name: Jean F. Heuler

Date: April 30, 2001

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, DC 20231

Dear Sir,

Please amend the above-identified application as follows:

In the Specification

Page 1, line 4, please add the following:

Related Application

The present application is a continuation of co-pending
application serial no. 08/075,032, filed June 10, 1993, the
disclosure of which is hereby incorporated, in its entirety,
herein by reference.

D-2929 CON

In the Claims

Cancel claims 10 to 16, without prejudice.

Amend claims 1 and 17 as follows:

1. (Amended) A method of treating a patient suffering from a neuromuscular disorder or condition, said method comprising administering simultaneously to the patient a therapeutically effective amount of at least two neurotoxins selected from a group consisting of botulinum toxin types A, B, C, D, E, F and G, an amount of each selected neurotoxin being selected to control a duration of therapeutic activity of the administered neurotoxins.

17. (Amended) A composition suitable for treating a patient suffering from a neuromuscular disorder or condition, said composition comprising a therapeutically effective amount of at least two neurotoxins selected from a group consisting of botulinum toxin types A, B, C, D, E, F and G, an amount of each selected neurotoxin being selected to control a duration of therapeutic activity of the neurotoxins.

Add new claim as follows:

26. (New) A composition suitable for treating a patient suffering from a neuromuscular disorder or condition, said composition comprising a therapeutically effective amount of at least two neurotoxins selected from a group consisting of botulinum toxin types A, B, C, D, E, F and derivative of G, an

Variable	Mean	SD	Min	Max
Age	34.5	10.2	22	55
Gender	0.5	0.5	0	1
Marital status	0.6	0.5	0	1
Education	12.5	1.5	9	16
Income	1500	500	500	3000
Health status	0.8	0.2	0	1
Employment status	0.7	0.3	0	1
Life satisfaction	4.5	1.0	1	7
Depression	0.3	0.5	0	1
Stress	3.5	1.5	1	6
Resilience	5.5	1.0	3	7
Optimism	4.0	1.0	1	7
Gratitude	5.0	1.0	1	7
Forgiveness	4.5	1.0	1	7
Empathy	5.5	1.0	1	7
Compassion	5.0	1.0	1	7
Kindness	5.5	1.0	1	7
Generosity	5.0	1.0	1	7
Patience	5.5	1.0	1	7
Self-control	5.0	1.0	1	7
Emotional stability	5.5	1.0	1	7
Psychological well-being	5.0	1.0	1	7
Life purpose	5.5	1.0	1	7
Meaning in life	5.0	1.0	1	7
Existential well-being	5.5	1.0	1	7
Transcendental well-being	5.0	1.0	1	7
Overall well-being	5.5	1.0	1	7

amount of each selected neurotoxin being selected to control a duration of therapeutic activity of the neurotoxins.

REMARKS

The above-identified application has been carefully reviewed in light of the February 28, 2001, Board's decision on the prior (parent) application serial no. 08/075,032, filed June 10, 1993.

Claims 10 to 16 have been canceled without prejudice.

Claims 1 and 17 have been amended to make clear that the different serotypes of botulinum toxin are simultaneously administered. Attached is a version of claims 1 and 17 with markings to show the amendments.

New claim 26 has been added. This claims is substantially similar to claim 17, with the addition of derivatives of type G.

The amended independent Claims 1 and 17, and their respective dependent claims 2 to 9 and 18 to 25, and new claim 26 are fully supported by the specification. For instance, Example 1 on page 11 of the specification discloses a patient being treated with a composition having both serotype toxin A and serotype toxin B. When such composition is administered according to Example 1, serotype toxins A and B can only be administered simultaneously.

The applicant further submits that the subject matters in pending claims 1 to 9 and 17 to 26 are novel at the priority filing date (June 10, 1993) of this application. Particularly, the administration of more than one serotype of botulinum toxin simultaneously is novel. That is, no one has administered more than one botulinum toxin simultaneously prior to June 10, 1993.

D-2929 CON

Additionally, the applicant submits that the subject matters in pending claims 1 to 9 and 17 to 26 are not obvious at the priority filing date of this application. To establish a prima facie case of obviousness under 35 U.S.C. §103, there must exist is a motivation found in the prior art to combine the prior art to arrive at the present invention. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988) and *In re Skinner*, 2 U.S.P.Q.2d, 1788, 1790 (Bd. Pat. App. & Int. 1986).

There is simply no disclosure, teaching or suggestion, explicitly or implicitly, in the prior art that would motivate one of ordinary skill in the art to administer two or more serotype toxins simultaneously, as is claimed in Claims 1 to 9. Likewise, the prior art is devoid of any disclosure, teaching or suggestion, explicitly or implicitly, which would motivate one of ordinary skill in the art to provide a composition comprising a therapeutically effective amount of at least two neurotoxins, as is claimed in Claims 17 to 26.

To the applicant's knowledge, the references that are most relevant to pending Claims 1 to 9 and 17 to 26 are Ludlow et al. *The New England Journal of Medicine*, Vol. 326(5), page 349, January 1992; Simpson, *Pharmacological Reviews*, Vol. 33(3), pages 155-158, 1981; and Jankovic and Brin, *The New England Journal of Medicine*, Vol. 324, pages 1186-1194, 1991.

However, these references, separately or in combination, may only at most suggest that a single, specific second toxin (serotype F) can be administered sequentially, after another single, specific first toxin (serotype A) ceases to be therapeutically effective. These references, separately or in combination, do not disclose, teach or even suggest that more than one serotype of botulinum toxin may be administered simultaneously.

D-2929 CON

One important advantage of administering at least two different serotype toxins simultaneously is that the "duration of therapeutic activity" can be controlled without having a second toxin administered sequentially, after the first toxin is no longer effective to provide a therapeutic effect. The prior art does not even suggest such an advantage. To the contrary, the teaching of only sequential administration of toxins actually teaches away from the present invention and the above-noted advantage achieved by appellant.

Therefore, applicant submits that the presently pending claims 1 to 9 and 17 to 26 are novel and unobvious, and are patentable.

Applicant respectfully requests early and favorable action in the above-identified application. Should any matters remain unresolved, the Examiner is requested to call applicant's attorney at the telephone number given below.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

1. (Amended) A method of treating a patient suffering from a neuromuscular disorder or condition, said method comprising administering simultaneously to the patient a therapeutically effective amount of [a combination of] at least two neurotoxins selected from a group consisting of botulinum toxin types A, B, C, D, E, F and G, an amount of each selected neurotoxin being selected to control a duration of therapeutic activity of the administered [combination] neurotoxins.

17. (Amended) A composition suitable for treating a patient suffering from a neuromuscular disorder or condition, said composition comprising a therapeutically effective amount of [a combination of] at least two neurotoxins selected from a group consisting of botulinum toxin types A, B, C, D, E, F and G, an amount of each selected neurotoxin being selected to control a duration of therapeutic activity of the [administered combination] neurotoxins.